Rejection under 35 USC §112

Claims 1 - 39 were rejected under 35 USC §112 as indefinite for use of the term "electronically addressable microchip." Applicants submit that the meaning of the term is sufficiently definite to one of ordinary skill in the analytical micro-electrical device arts, given the present specification and drawings, and the commonly owned disclosures, e.g., WO96/01836, which were known to those of skill in the art at the time the present application was filed. However, in order to improve clarity, the applicants have reiterated in the claim the basic elements of the electronically addressable microchip, namely "a plurality of electronically programmable microlocations, wherein the microlocations each comprise an underlying working microelectrode on a substrate, wherein at least some of the microelectrodes are covered by a permeation layer." Applicants submit that this language is sufficiently definite, especially considering the context given to the claim language by the specification and drawings. Thus, applicants respectfully request that this rejection be reconsidered and withdrawn.

In addition, claims 6, 19, 26, 35, and 39 were rejected as indefinite for the use of electronic terms without defining "what addressing has occurred." Applicants believe that the clear recitation of the electrodes in the array structure and the recitation of the application of a potential to those electrodes (providing the electron transfer to/from water to change the pH) is sufficiently definite for those of ordinary skill in the chemical arts. Applicants thus respectfully request that this rejection be reconsidered and withdrawn.

Claims 1 and subsequent claims 2-39 (and more specifically 28) were rejected as indefinite because the "permeation layer" recitation was said not to relate structurally to the other elements of the claim. Similarly, the recitation of "permeable polymer" in claim 21 was objected to. Applicants submit that the position of the permeation layer with respect to the electronically addressable microarray device is sufficiently clear in the claims as amended, as is the relation of the chemical moieties as chemically integrated sub-parts of the permeation layer structure. Applicants thus respectfully request that these rejections be reconsidered and withdrawn.

Claim 2 was rejected as indefinite for the use of the term "including but not limited to." Applicants have eliminated this language, and have instead merely listed the α,β unsaturated carbonyls as alternative groups, which are a sub-set of the broader term "alkenyl moieties."

Applicants submit that the claims, as amended, are clear, and respectfully request the reconsideration and withdrawal of this rejection.

Applicants have also amended the first group of claims (1-13) to replace the references to the P', X', and R' moieties with second (and further) P-X-R groups. Applicants note that additional moieties with the same general structure or characteristics are often designated in chemical practice utilizing a prime ('), double prime ("), etc. However, in order to simplify the language of the claims, the applicants have changed the wording to simply first and second P-X-R groups. Applicants thus submit that the claims, as amended, are definite, and respectfully request that this rejection be reconsidered and withdrawn.

Applicants have made further amendments to clarify the polymerizable moieties which may be utilized as "P" moieties. Applicants have amended the claims to recite smaller alternative moiety groups for P, as noted on page 14 and throughout the specification. In addition, applicants have made amendments to change the term "chemical bond," as used in the claims, to "covalent bond," which is in better accord with common usage in the chemical arts. Applicants note that this meaning of the term is apparent from its usage in the definitions on page 15 for X and R, especially when read in light of, e.g., Example 6c on page 42.

I. 35 USC 102(e) Rejections

Claims 1 - 4, and 13 were rejected as anticipated under 35 U.S.C. 102(e) by the Heller patent, USP 5,632,957 (the '957 patent). Claims 1-4, 7, 10, 13-17, 21-23, 28, 30, 32, and 38 were rejected as anticipated under 35 U.S.C. 102(e) by the Sundberg patent, USP 5,919,523 (the '523 patent). In order to anticipate a claim, a reference must disclose each and every element and limitation of that claim, MPEP §2131. Applicants submit that neither reference discloses each and every limitation of the claimed invention, and thus neither patent can anticipate the claimed invention under 35 USC 102(e).

The '957 patent is said to anticipate the claimed invention based on its disclosure of a Nafion/polylysine "two layer ionomer sandwich" permeation layer over electrodes at microlocations of a bioelectronic array device. The Nafion layer was asserted to be the "P" of a claimed P-X-R group, and the poly-lysine layer was asserted to provide both an "R" functional group for biomolecular attachment (in the form of a primary amine for coupling) and "the X

bond of the instant claims." Applicants respectfully traverse this characterization of the structure disclosed in the '957 patent, and submit that the disclosed structure is lacking the explicitly recited limitations of the claims.

Nafion is a perflorinated sulfonic acid electrolyte compound, which was cast onto the microlocation, and allowed to dry. The poly-lysine layer is merely adsorbed onto the Nafion layer (see column 18, lines 44-45). No covalent bond is formed between the Nafion layer and the poly-lysine layer. The structure of the P-X-R groups clearly requires that X be at least a covalent bond between the P and R moieties, and that the P, X, and R elements are linked into a chemical group structure. Thus, the recited two-layer ionic structure from the '957 does not resemble the structure recited in the claims. Thus, the applicants submit that the '957 patent does not anticipate claim 1-4 and 13, and respectfully requests that the 102(e) rejection be reconsidered and withdrawn.

Applicants also respectfully submit that the invention, as claimed, is not disclosed in the '523 Patent. First, the Sundberg reference was offered with "the interpretation that the electronic addressability wording in the preamble is not a claim limitation per se." Applicants submit that the claims, as amended, clearly require that the array device comprise electrodes at microlocations under a permeation layer. None of this recited structure is present in the arrays of disclosed in the Sundberg reference. In fact, applicants submit that the polymer layers coating the silica substrate in the column 2 structure cited in the Office action form a thin coating layer, which would not function to allow the free exchange of ions and small molecules through the layer while insulating the attached biomolecules from an electrode at the substrate surface. Thus, applicants submit that the claimed invention is not disclosed in the '523 patent, and respectfully request the reconsideration and withdrawal of this rejection.

Applicants note that claims 5, 6, 11, 12, 18, 19, 24 - 26, 29, 31, and 33-37 were not rejected under 35 USC §102 or §103, and thus appear to have been found free of the prior art. Applicants therefore submit that these claims are in a position for allowance, as the amendments to the claims should have resolved all cited §112 rejections.

II. Conclusions

Applicants submit that the claimed invention is a substantial improvement in the previously disclosed permeation layer technologies. As demonstrated in the data from the examples, the claimed methods offer significant improvements in the integration of biomolecular attachment sites into the permeation layer in a more uniform fashion. Applicants submit that the claims, as amended, are in position for allowance, and thus request favorable consideration..

Should any additional fees be required with the present filing, please charge or credit our Deposit Account No. 12-2475 for the appropriate amount.

Respectfully submitted,

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Date: July 26, 2001

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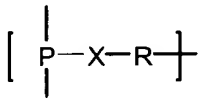
MARKED-UP VERSION OF CLAIMS

U.S. APPLICATION NO. 09/410,368

We Claim:

1. An electronically addressable [~~microarray with~~] microchip device comprising a plurality of electronically programmable microlocations, wherein the microlocations each comprise an underlying working microelectrode on a substrate, wherein at least some of the microelectrodes are covered by a permeation layer [~~containing~~] comprising at least first chemical group[~~s~~] for attaching to the microarray [~~biomolecules and/or second chemical groups, said first groups~~] biomolecules, the first group having the formula:



[~~P-X-R~~]

wherein,

P is a [~~chemical moiety for binding to the microarray and/or for binding a moiety of said second chemical~~] polymerizable moiety covalently attached to the permeation layer matrix and/or covalently attached to one or more other P-X-R groups, as defined herein, wherein the other P-X-R group may be the same as or different from the first P-X-R group;

X is a [~~chemical bond or a linking chemical moiety~~] covalent bond or a linking moiety; and

R is a [~~chemical moiety for attaching, either covalently or non-covalently, a derivatized biomolecule, or for attaching covalently a moiety of said second chemical groups.~~] functional moiety for attaching, either covalently or non-covalently, a derivatized biomolecule, or for attaching covalently an other P-X-R group, as defined herein, wherein the other P-X-R group may be the same as or different from the first P-X-R group, and wherein R may, optionally, be attached to a biomolecule or an other P-X-R group.

2. The microarray of claim **1** wherein ℙ is selected from the group consisting of, alkenyl, α,β,unsaturated carbonyl, vinyl, allyl and homoallyl moieties. [~~A microarray according to claim 1 wherein ℙ is selected from the group consisting of, alkenyl moieties including but not limited to α,β,unsaturated carbonyls vinyl, allyl and homoallyl groups; epoxide, a chemical bond, phenyl boronic acid, salicylic hydroxamic acid, acetal, ester, carboxylic acid, amide, halo-acetamide, thiol, phosphorothiolate monoester, thioester, disulfide, aldehyde, ketone, hydrazide, hydrazine, and amines.~~]

3. The microarray of claim **1** wherein ℝ is selected from the group consisting of a covalent bond, streptavidin, a portion of streptavidin, biotin, phenyl boronic acid, salicylic hydroxamic acid, vinyl, allyl, homoallyl, acetal, ester, carboxylic acid, amide, halo-acetamide, thiol, phosphorothiolate monoester, thioester, disulfide, aldehyde, ketone, hydrazide, hydrazine, and amine moieties. [~~A microarray according to claim 1 wherein ℝ is selected from the group consisting of a chemical bond, streptavidin, a portion of streptavidin, biotin, phenyl boronic acid, salicylic hydroxamic acid, vinyl, allyl, homoallyl, acetal, ester, carboxylic acid, amide, halo-acetamide, thiol, phosphorothiolate monoester, thioester, disulfide, aldehyde, ketone, hydrazide, hydrazine, and amines.~~]

4. The microarray of claim **1** wherein ℝ is a moiety that requires an activating step prior to participating in a chemical reaction for binding either a derivatized biomolecule or a moiety of an other P-X-R group. [~~A microarray according to claim 1 wherein ℝ is a chemical moiety that is activated prior to participating in a chemical reaction for binding either a derivatized biomolecule or a moiety of said second chemical group.~~]

5. The microarray of claim **4** wherein ℝ requires activation by either basic or acidic conditions. [~~A microarray according to claim 4 wherein said ℝ is activated by either an increase or decrease in pH of a solution overlying said ℝ.~~]

6. The microarray of claim **5** wherein the basic or acidic condition necessary to active ℝ may be produced by applying an electronic potential at at least one electrode of the electronically addressable microarray. [~~A microarray according to claim 5 wherein said pH change is provided~~

~~by an electronically generated potential of an electrode of an electronically addressable microarray.~~]

7. The microarray of claim **1** wherein ℙ is covalently attached to at least one other P-X-R group, further wherein the ℙ is covalently attached to the ℙ moiety of the at least one other P-X-R group. [~~A microarray according to claim 1 wherein ℙ is further bonded with said second chemical groups wherein said second chemical groups have the formula ℙ'-X'-ℝ', further wherein said ℙ is bonded to the ℙ' moiety of at least one said second chemical group.~~]

8. The microarray of claim **7** wherein the at least one other P-X-R group is a portion of a polymer, wherein a backbone of the polymer comprises the ℙ moieties of a plurality of P-X-R groups covalently attached to one another. [~~A microarray according to claim 7 wherein said second chemical groups form a polymer wherein a backbone of said polymer comprises ℙ' moieties connected to one another and -X'-ℝ' are connected to each ℙ'.~~]

9. The microarray of claim **8** wherein the P and/or R moieties of the first P-X-R group and the P-X-R groups in the polymer backbone are the same. [~~A microarray according to claim 8 wherein ℙ' equals ℙ, X' equals X, and/or ℝ' equals ℝ.~~]

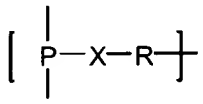
10. The microarray of claim **1** wherein ℝ is covalently attached to an other P-X-R group, further wherein the ℝ is covalently attached the ℙ moiety of the other P-X-R group. [~~A microarray according to claim 1 wherein ℝ is bonded with said second chemical groups wherein said second chemical groups have the formula ℙ'-X'-ℝ', further wherein said ℝ is bonded to the ℙ' moiety of at least one said second chemical group.~~]

11. The microarray of claim **10** wherein the other P-X-R group is a portion of a polymer, wherein a backbone of the polymer comprises a plurality of P-X-R groups covalently attached to one another by P-R covalent attachments. [~~A microarray according to claim 10 wherein said second chemical groups form a polymer wherein a backbone of said polymer comprises ℙ' moieties connected to one another and -X'-ℝ' are connected to each ℙ'.~~]

12. The microarray of claim 11 wherein the P and/or R moieties of the first P-X-R group and the P-X-R groups in the polymer backbone are the same. [~~A microarray according to claim 11 wherein P' equals P, X' equals X, and/or R' equals R.~~]

13. The microarray of claim 1 wherein X is selected from the group consisting of a covalent bond, an alkyl group of 1-10 carbon atoms, an alkenyl group of 2-10 carbon atoms, alkyl esters, ketones , amides, ethers, thioesters, amido groups, and carbonyls, and any combinations thereof. [~~A microarray according to claim 1 wherein X is selected from the group consisting of a chemical bond, an alkyl group of 1-10 carbon atoms, an alkenyl group of 2-10 carbon atoms, alkyl esters, ketones , amides, ethers, thioesters, amido groups, and carbonyls, and any combinations thereof.~~]

14. An electronically addressable microchip device comprising a plurality of electronically programmable microlocations, wherein the microlocations each comprise an underlying working microelectrode on a substrate, wherein at least some of the microelectrodes are covered by a permeation layer comprising first and second chemical groups having the formula



wherein,

P is a polymerizable moiety [~~chemical moiety for binding to the microarray, each of said P moieties further connecting said first groups to a permeable polymer of said microarray and to at least one P' of said second groups, said P' moieties each further connecting at least one other P' moiety of said second groups to form a polymer of said second groups~~];

X is a linking moiety [~~and X' are linking chemical moieties~~] selected from the group consisting of a [~~chemical~~] covalent bond, an alkyl group of 1-10 carbon atoms, an alkenyl group of 2-10 carbon atoms, alkyl esters, ketones, ethers amides, thioesters, amido groups, and carbonyls, and any combinations thereof; and

ℝ is a functional moiety [~~and ℝ' are chemical moieties~~] for attaching, either covalently or non-covalently, a derivatized biomolecule;
wherein the first and second P-X-R groups may be the same or different;
wherein the ℙ moieties of the first P-X-R group are covalently attached to the permation layer matrix and to at least one ℙ of the second P-X-R groups;
and wherein the ℙ moieties of the second P-X-R groups are covalently attached to at least one other ℙ moiety of another second P-X-R groups to form a polymer of the second P-X-R groups.

15. The microarray of [~~A microarray according to~~] claim 14 wherein ℝ [~~and ℝ' are~~] for the first and second P-X-R groups are, independently, selected from the group consisting of streptavidin, a portion of streptavidin, biotin, [~~PBA, SHA,~~] phenyl boronic acid, salicylic hydroxamic acid, vinyl, allyl, homoallyl, acetal, ester, carboxylic acid, amide, halo-acetamide, thiol, phosphorothiolate monoester, thioester, disulfide, aldehyde, ketone, hydrazide, hydrazine, and amines.

16. [~~A microarray according to claim 15 wherein ℝ equals ℝ'.~~] The microarray of claim 15 wherein ℝ are the same for the first and second P-X-R groups.

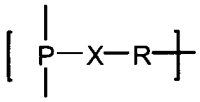
17. [~~A microarray according to claim 14 wherein said ℙ or ℙ' and ℝ or ℝ' are chemical moieties that are activated~~] The microarray of claim 14 wherein ℙ of the first and/or second P-X-R groups require activation prior to participating in a [~~chemical reaction which~~] polymerization reaction, wherein the activation is either under the same or mutually exclusive conditions. [~~, wherein said chemical reaction is between any of combinations of ℙ and ℙ', ℝ and a derivatized biomolecule, and/or ℙ' and ℙ' of another second group.~~]

18. The [A] microarray of [according to] claim 17 wherein [~~said ℙ, ℝ, ℙ' or ℝ' are activated by either an increase or decrease in pH of a reaction solution overlying said microarray.~~] the activation is by basic or acidic conditions.

19. The [~~A~~] microarray of [~~according to~~]-claim 18 wherein the basic or acidic conditions required for activation may be produced by applying an electronic potential at at least one electrode of the electronically addressable microarray. [~~said pH change is provided by an electronically generated potential of an electrode of an~~]

20. [Cancelled].

21. An electronically addressable [~~microarray containing a permeation layer with first chemical groups and second chemical groups, said first groups having the formula P-X-R and said second groups having the formula P'-X'-R'~~] microchip device comprising a plurality of electronically programmable microlocations, wherein the microlocations each comprise an underlying working microelectrode on a substrate, wherein at least some of the microelectrodes are covered by a permeation layer comprising first P-X-R groups and second P-X-R groups having the formula:



wherein,

P is a [~~chemical moiety for direct binding to the microarray, each of said P moieties further connecting said first groups to a permeable polymer of said microarray, said R is a chemical moiety connecting to at least one P' of said second groups, said P' moieties each further connecting at least one other P' moiety of said second groups to form a polymer of said second groups;~~] polymerizable moiety; ~~—~~

X [~~nd X' are linking chemical moieties~~] is a linking moiety selected from the group consisting of a [~~chemical~~] covalent bond, an alkyl group of 1-10 carbon atoms, an alkenyl group of 2-10 carbon atoms, alkyl esters, ketones, ethers amides, [~~ethers,~~] thioesters, amido groups, and carbonyls, and any combinations thereof; and

R is a functional [~~R' is a chemical~~] moiety for attaching, either covalently or non-covalently, a derivatized biomolecule;

wherein the first and second P-X-R groups may be the same or different;

wherein the ℙ of the first P-X-R group are covalently attached to the permeation layer matrix

wherein the ℝ of the first P-X-R group is covalently attached to at least one ℙ of the second P-X-R groups;

and wherein the ℙ of the second P-X-R groups are covalently attached to at least one other ℙ of another second P-X-R groups to form a polymer of the second P-X-R groups.

22. The [~~A~~]-microarray [according to] of claim **21** wherein ℝ [~~and ℝ' are~~] for the first and second P-X-R groups are, independently, selected from the group consisting of streptavidin, a portion of streptavidin, biotin, phenyl boronic acid, salicylic hydroxamic acid, vinyl, allyl, homoallyl, acetal, ester, carboxylic acid, amide, halo-acetamide, thiol, phosphorothiolate monoester, thioester, disulfide, aldehyde, ketone, hydrazide, hydrazine, and amines.

23. The [~~A~~]-microarray of [according to] claim **22** wherein [~~ℝ equals ℝ'.~~] ℝ is the same for the first and second P-X -R groups.

24. The [~~A~~]-microarray of [according to] claim 21 wherein [~~said ℙ or ℙ' and ℝ or ℝ' are chemical moieties that are activated prior to participating in a chemical reaction~~] the ℙ or ℝ of the first and/or second P-X-R groups require activation prior forming a covalent bond between the ℙ and ℝ of the first and second group, wherein the activation is either under the same or mutually exclusive condition. [~~wherein said chemical reaction is between any of combinations of ℙ and ℙ', ℝ and ℙ', and ℙ' and ℙ' of another second group.~~]

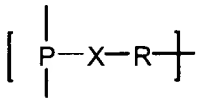
25. The [A] microarray of [according to] claim **24** wherein [~~said ℙ, ℝ, ℙ' or ℝ' are activated by either an increase or decrease in pH of a solution overlying said microarray.~~] the activation is by basic or acidic conditions.

26. ~~A microarray according to claim 25 wherein said pH change is provided by an electronically generated potential of an electrode of an~~The microarray of claim **25** wherein the

basic or acidic conditions required for activation may be produced by applying an electronic potential at at least one electrode of the electronically addressable microarray.

27. [Cancelled.]

28. An electronically addressable microchip device comprising a plurality of electronically programmable microlocations, wherein the microlocations each comprise an underlying working microelectrode on a substrate, wherein at least some of the microelectrodes are covered by a permeation layer comprising a first P-X-R group attached to biomolecules and/or to polymerized monomer units comprising second P-X-R groups, wherein the polymerized second P-X-R groups are further attached to biomolecules, wherein the attachment of the biomolecules to the first P-X-R groups or to the polymerized second P-X-R groups requires activation of at least one of the first and/or the second P-X-R groups under acidic and/or basic pH conditions, wherein the first and second P-X-R groups have the formula



wherein,

$\mathbb{P}$ is a polymerizable moiety,

$\mathbb{X}$ is a linking moieties selected from the group consisting of a covalent bond, an alkyl group of 1-10 carbon atoms, an alkenyl group of 2-10 carbon atoms, alkyl esters, ketones, ethers amides, thioesters, amido groups, and carbonyls, and any combinations thereof; and

$\mathbb{R}$ is a functional moiety for attaching, either covalently or non-covalently, a derivatized biomolecule or for attaching covalently an other P-X-R group;

wherein $\mathbb{P}$ comprises a chemical element requiring activation for attaching to the permeation layer and/or to a $\mathbb{P}$ of an other P-X-R group;

and wherein $\mathbb{R}$ comprises chemical elements requiring activation different from $\mathbb{P}$ of either the first or second P-X-R groups for attaching the biomolecules, or to $\mathbb{P}$ of another P-X-R groups.

[~~An electronically addressable microarray having a permeation layer having first chemical moieties attached to biomolecules and/or to polymerized monomer units comprising second~~

~~chemical moieties, said second chemical moieties further attached to biomolecules, wherein said attachment of said biomolecules to said first chemical moieties or to said polymerized units has occurred following activation of at least one of said first and/or said second chemical moieties under acidic and/or basic pH conditions, said first chemical moieties have the formula P-X-R and said second chemical moieties having the formula P'-X'-R', wherein said P comprises a chemical element requiring activation for attaching to said permeation layer and/or to a P' of said second chemical moiety, said X and X' comprise nonreactive chemical elements, and said R and R' comprise chemical elements requiring activation different from P and P' for attaching said biomolecules or to P' of another second chemical moiety.~~]

29. The microarray of claim **28** wherein the permeation layer comprises a polymer polymerized from a monomer selected from the group consisting of acrylamide, bisacrylamide, methacrylamide, *N*-alkyl acrylamides, functionalized ethylene glycol derivatives, *N*-vinyl pyrrolidinone, bis-cystamine, acrylates, methacrylates, and acrylonitriles. [~~A microarray of claim 28 wherein said permeation layer comprises a polymer polymerized from the monomer group consisting of acrylamide, bisacrylamide, methacrylamide, *N* alkyl acrylamides, functionalized ethylene glycol derivatives, *N* vinyl pyrrolidinone, bis-cystamine, acrylates, methacrylates, and acrylonitriles where alkyl refers to a carbon chain.~~]

30. The microarray of claim **28** wherein the biomolecules are derivatized with a chemical moiety selected from the group consisting of vinyl, allyl, homoallyl, acetal, ester, carboxylic acid, amide, halo-acetamide, thiol, phosphorothiolate monoester, thioester, disulfide, aldehyde, ketone, hydrazide, hydrazine, and amines. [~~A microarray of claim 28 wherein said biomolecules are derivatized with a chemical moiety selected from the group consisting of vinyl, allyl, homoallyl, acetal, ester, carboxylic acid, amide, halo-acetamide, thiol, phosphorothiolate monoester, thioester, disulfide, aldehyde, ketone, hydrazide, hydrazine, and amines.~~]

31. The microarray of claim **28** wherein P for the first and second P-X-R groups are, independently, selected from the group consisting of alkenyl moieties, α,β,unsaturated carbonyls, vinyl, allyl and homoallyl groups, acetal, thioester, disulfide, epoxides, alkyl ether, and carboxylic acid moieties. [~~A microarray of claim 28 wherein said P and P' are selected from~~

~~the group consisting of alkenyl moieties, α,β,unsaturated carbonyls, vinyl, allyl and homoallyl groups, acetal, thioester, disulfide, epoxides, alkyl ether, and carboxylic acid.~~]

32. The microarray of claim **28** wherein the X for the first and second P-X-R groups are, independently, selected from the group consisting of a covalent bond, a carbon chain consisting of 1 to 10 carbons, ethers, polyethers, amides, and esters. [~~A microarray of claim **28** wherein said X and X' are selected from the group consisting of a chemical bond, a carbon chain consisting of 1 to 10 carbons, ethers,~~ polyethers, amides, and esters.]

33. The microarray of claim **28** wherein the ℝ for the first and second P-X-R groups are, independently, selected from the group consisting of alkenyl moieties, α,β,unsaturated carbonyls, vinyl, allyl, homoallyl, acetal, ester, carboxylic acid, thioester, disulfide, epoxide, and alkyl ether moieties. [~~A microarray of claim **28** wherein said ℝ and ℝ' are selected from the group consisting of alkenyl moieties, α,β,unsaturated carbonyls, vinyl, allyl, homoallyl, acetal, ester, carboxylic acid, thioester, disul~~fide, epoxide, and alkyl ether.]

34. The microarray of claim **33** wherein the ℝ is the same for the first and second P-X-R groups. [~~A microarray of claim **33** wherein said ℝ equals ℝ'.~~]

35. The microarray of claim **28** wherein the acidic or basic conditions are produced by a method selected from the group consisting of: contacting the electronic microarray with a buffer of the appropriate pH, applying an electronic potential at at least one electrode of the electronically addressable microarray to alter the pH, and a combination of the two methods. [~~An microarray of claim **28** wherein adjustment of pH has been initiated by lowering or raising the pH of the buffer and/or by biasing electrodes of said electronically addressable array with either positive or~~ negative electronic potential.]

36. The microarray of claim **28** wherein ℝ for the first and second P-X-R groups are thioester moieties. [~~A microarray according to claim **28** wherein each of said ℙ, ℙ', ℝ, and or ℝ' is a thioester.~~]

37. The microarray of claim **28** wherein ℝ for the first and second P-X-R groups are acetal moieties. [~~A microarray according to claim 28 wherein each said ℙ, ℙ', ℝ, and or ℝ'~~ is an acetal moiety.]

38. The microarray of claim **28** wherein the ℝ is selected from the group consisting of derivatized amine, salicyl hydroxamic acid, bromoacetamide, salicyl hydroxamic acid, maleimide, streptavidin, biotin, vinyl, allyl, homoallyl, acetal, ester, carboxylic acid, amide, halo-acetamide, thiol, phosphorothiolate monoester, thioester, disulfide, aldehyde, ketone, hydrazide, hydrazine, and amine moieties. [~~A microarray according to claim 28 wherein said ℝ is selected from the group consisting of amines, derivatized amines, salicylhydroxamic acid, bromoacetamide, salicyl hydroxamic acid, maleimide, streptavidin, biotin, vinyl, allyl, homoallyl, acetal, ester, carboxylic acid, amide, halo-acetamide, thiol, phosphorothiolate monoester, thioester, disulfide, aldehyde, ketone, hydrazide, hydrazine, and amines.~~]

39. The microarray of claim **35** wherein the electronic potential used to alter the pH is applied at a current density of between 50 nA/5000μm^2 and 5 μA/5000μm^2 at the at least one electrode for a time period between 30 and 600 seconds. [~~A microarray according to claim 35 wherein said electronic potential has been applied at a current density of between 50 nA/5000μm^2 and 5 μA/5000μm^2 at a site on the microarray intended for activation for a time period between 30 and 600 seconds.~~

NEW CLAIMS

67. The microarray of claim **1** wherein ℙ is selected from the group consisting of an acetal, epoxide, ester, carboxylic acid, amide, halo-acetamide, thiol, phosphorothiolate monoester, thioester, disulfide, aldehyde, ketone, hydrazide, hydrazine, and amine moieties.

68. The microarray of claim **1** wherein ℝ is selected from the group consisting of streptavidin, a portion of streptavidin, and biotin.

69. The microarray of claim **1** wherein ℝ is selected from the group consisting of aldehyde, ketone, amine, hydrazine, hydrazide, haloacetamide, epoxide, thiol, phosphorothiolate monoester, and ester moieties.

70. The microarray of claim **1** wherein **R** is selected from the group consisting of phenyl boronic acid and salicylic hydroxamic acid.

71. The microarray of claim **1** wherein **R** is selected from the group consisting of disulfide, thioester, tertiary carbon, alkene, alkyl ether, acetal, and carboxylic acid.

72. The microarray of claim **14** wherein **P** is selected from the group consisting of, alkenyl, α,β,unsaturated carbonyl, vinyl, allyl and homoallyl moieties.

73. The microarray of claim **14** wherein **P** is selected from the group consisting of an acetal, epoxide, ester, carboxylic acid, amide, halo-acetamide, thiol, phosphorothiolate monoester, thioester, disulfide, aldehyde, ketone, hydrazide, hydrazine, and amine moieties.

74. The microarray of claim **14** wherein **R** is selected from the group consisting of streptavidin, a portion of streptavidin, and biotin.

75. The microarray of claim **14** wherein **R** is selected from the group consisting of aldehyde, ketone, amine, hydrazine, hydrazide, haloacetamide, epoxide, thiol, phosphorothiolate monoester, and ester moieties.

76. The microarray of claim **14** wherein **R** is selected from the group consisting of phenyl boronic acid and salicylic hydroxamic acid.

77. The microarray of claim **14** wherein **R** is selected from the group consisting of disulfide, thioester, tertiary carbon, alkene, alkyl ether, acetal, and carboxylic acid.

78. The microarray of claim **14** wherein the **R** moieties of the first and/or second P-X-R groups require activation prior to covalent attachment to a biomolecule, wherein the activation is either under the same or mutually exclusive conditions for the first and second groups.

79. The microarray of claim **78** wherein the activation is by basic or acidic conditions.

80. The microarray of claim **79** wherein the basic or acidic conditions required for activation may be produced by applying an electronic potential at at least one electrode of the electronically addressable microarray.

81. The microarray of claim **21** wherein **P** is selected from the group consisting of, alkenyl, α,β,unsaturated carbonyl, vinyl, allyl and homoallyl moieties.

82. The microarray of claim **21** wherein **P** is selected from the group consisting of an acetal, epoxide, ester, carboxylic acid, amide, halo-acetamide, thiol, phosphorothiolate

monoester, thioester, disulfide, aldehyde, ketone, hydrazide, hydrazine, and amine moieties.

83. The microarray of claim **21** wherein **R** is selected from the group consisting of streptavidin, a portion of streptavidin, and biotin.

84. The microarray of claim **21** wherein **R** is selected from the group consisting of aldehyde, ketone, amine, hydrazine, hydrazide, haloacetamide, epoxide, thiol, phosphorothiolate monoester, and ester moieties.

85. The microarray of claim **21** wherein **R** is selected from the group consisting of phenyl boronic acid and salicylic hydroxamic acid.

86. The microarray of claim **21** wherein **R** is selected from the group consisting of disulfide, thioester, tertiary carbon, alkene, alkyl ether, acetal, and carboxylic acid.

87. The microarray of claim **1** wherein the permeation layer comprises a polymer polymerized from a monomer selected from the group consisting of acrylamide, bisacrylamide, methacrylamide, *N*-alkyl acrylamides, functionalized ethylene glycol derivatives, *N*-vinyl pyrrolidinone, bis-cystamine, acrylates, methacrylates, and acrylonitriles.

88. The microarray of claim **14** wherein the permeation layer comprises a polymer polymerized from a monomer selected from the group consisting of acrylamide, bisacrylamide, methacrylamide, *N*-alkyl acrylamides, functionalized ethylene glycol derivatives, *N*-vinyl pyrrolidinone, bis-cystamine, acrylates, methacrylates, and acrylonitriles.

89. The microarray of claim **21** wherein the permeation layer comprises a polymer polymerized from a monomer selected from the group consisting of acrylamide, bisacrylamide, methacrylamide, *N*-alkyl acrylamides, functionalized ethylene glycol derivatives, *N*-vinyl pyrrolidinone, bis-cystamine, acrylates, methacrylates, and acrylonitriles.